PMA P030028

QUESTIONS FOR PANEL DISCUSSION

1. In a paired analysis, the percent change calculated between baseline and 3 years postop was -4.76% with a standard deviation of 7.8%. When analyzed by interval one can see that losses appear to be higher between the second and third postoperative years at -2.37% as compared to the interval between years one and two, -1.12%. The sponsor has presented the following endothelial cell loss data:

Overall Endothelial Cell Density Results
Cell Count Means

Least Squares Means						
Visit	**N**	**Estimate**	**Standard Deviation**	**Standard Error**	**95% Confidence Limits**	
PreOp	183	2754.2380	357.770	26.4471	2702.4020	2806.0730
6 Months	188	2747.5960	373.622	27.2492	2694.1890	2801.0040
1 Year	240	2711.3210	412.006	26.5949	2659.1960	2763.4460
2 Years	285	2680.1730	445.398	26.3831	2628.4630	2731.8830
3 Years	248	2605.2770	429.856	27.2959	2551.7780	2658.7760

Percent Change from Baseline

Least Squares Means						
Visit	**N**	**Estimate**	**Standard Deviation**	**Standard Error**	**95% Confidence Limits**	
6 Months	139	-0.0036	0.068	0.0058	-0.0149	0.0077
1 Year	134	-0.0106	0.068	0.0059	-0.0223	0.0011
2 Years	135	-0.0255	0.074	0.0064	-0.0379	-0.0130
3 Years	107	-0.0476	0.078	0.0075	-0.0623	-0.0328

Percent Change by Period

Least Squares Means						
Period	**N**	**Estimate**	**Standard Deviation**	**Standard Error**	**95% Confidence Limits**	
1Y-6M	149	-0.0117	0.062	0.0051	-0.0217	-0.0017
2Y-1Y	198	-0.0112	0.058	0.0041	-0.0192	-0.0033
3Y-2Y	**216**	**-0.0237**	0.063	0.0043	-0.0322	-0.0153
6M-BL	139	-0.0039	0.072	0.0061	-0.0158	0.0080
3y-6m	111	-0.0475	0.073	0.0069	-0.0610	-0.0341

Recount Sub-Study: All Data

Average Loss Over Time	-49.76 Cells/Year 95% CI = (-60.69, -38.83)
Projected 10 Years	**2267.43**
Projected 20 Years	**1769.81**
Projected 30 Years	**1272.18**

The endothelial cell loss results for the overall analysis stratified by Anterior Chamber Depth is presented in the following table:

Overall Endothelial Cell Density Results By Anterior Chamber Depth
Percent Change From Baseline

Least Squares Means							
Visit	ACD	N	Estimate	Standard Deviation	Standard Error	95% Confidence Limits	
6 Months	3.0 to 3.2mm	8	-0.0234	0.027	0.0095	-0.0421	-0.0048
6 Months	> 3.2 to 3.4mm	20	-0.0288	0.076	0.0171	-0.0623	0.0047
6 Months	> 3.4 to 3.9mm	67	-0.0028	0.059	0.0072	-0.0170	0.0113
6 Months	> 3.9	44	0.0113	0.062	0.0093	-0.0068	0.0295
1 Year	3.0 to 3.2mm	4	-0.0264	0.017	0.0083	-0.0428	-0.0101
1 Year	> 3.2 to 3.4mm	24	-0.0461	0.061	0.0125	-0.0705	-0.0217
1 Year	> 3.4 to 3.9mm	63	0.0031	0.065	0.0082	-0.0131	0.0192
1 Year	> 3.9	43	-0.0087	0.056	0.0085	-0.0254	0.0079
2 Years	3.0 to 3.2mm	8	-0.0076	0.037	0.0131	-0.0333	0.0182
2 Years	> 3.2 to 3.4mm	22	-0.0373	0.076	0.0163	-0.0694	-0.0053
2 Years	> 3.4 to 3.9mm	67	-0.0272	0.068	0.0083	-0.0434	-0.0110
2 Years	> 3.9	38	-0.0197	0.066	0.0107	-0.0406	0.0012
3 Years	**3.0 to 3.2mm**	**6**	**-0.0916**	0.024	0.0098	-0.1108	-0.0725
3 Years	> 3.2 to 3.4mm	21	-0.0572	0.073	0.016	-0.0885	-0.0259
3 Years	> 3.4 to 3.9mm	52	-0.0412	0.079	0.0109	-0.0627	-0.0198
3 Years	> 3.9	28	-0.0471	0.060	0.0113	-0.0692	-0.0249

Overall Endothelial Cell Density Results By Anterior Chamber Depth
Percent Change By Period

Period	ACD	N	Estimate	Standard Deviation	Standard Error	95% Confidence Limits	
						Least Squares Means	
1Y-6M	3.0 to 3.2mm	7	-0.0171	0.018	0.0068	-0.0304	-0.0039
1Y-6M	> 3.2 to 3.4mm	23	-0.0187	0.060	0.0125	-0.0432	0.0058
1Y-6M	> 3.4 to 3.9mm	74	-0.0038	0.066	0.0077	-0.0190	0.0113
1Y-6M	> 3.9	45	-0.0195	0.054	0.0081	-0.0355	-0.0035
2Y-1Y	3.0 to 3.2mm	5	0.0255	0.036	0.0162	-0.0062	0.0573
2Y-1Y	> 3.2 to 3.4mm	30	-0.0046	0.055	0.0101	-0.0245	0.0152
2Y-1Y	> 3.4 to 3.9mm	100	-0.0182	0.051	0.0051	-0.0282	-0.0082
2Y-1Y	> 3.9	63	-0.0056	0.062	0.0078	-0.0210	0.0097
3Y-2Y	3.0 to 3.2mm	5	-0.0774	0.042	0.019	-0.1147	-0.0401
3Y-2Y	> 3.2 to 3.4mm	39	-0.0326	0.072	0.0115	-0.0551	-0.0100
3Y-2Y	> 3.4 to 3.9mm	116	-0.0177	0.058	0.0054	-0.0282	-0.0072
3Y-2Y	> 3.9	56	-0.0242	0.061	0.0081	-0.0401	-0.0083
6M-BL	3.0 to 3.2mm	8	-0.0344	0.048	0.017	-0.0678	-0.0010
6M-BL	> 3.2 to 3.4mm	20	-0.0302	0.110	0.0245	-0.0781	0.0178
6M-BL	> 3.4 to 3.9mm	67	0.0018	0.052	0.0064	-0.0108	0.0143
6M-BL	> 3.9	44	0.0057	0.066	0.0099	-0.0136	0.0250
3Y-6M	**3.0 to 3.2mm**	**7**	**-0.0899**	0.047	0.0177	-0.1246	-0.0552
3Y-6M	**> 3.2 to 3.4mm**	**22**	**-0.0295**	0.068	0.0145	-0.0580	-0.0010
3Y-6M	**> 3.4 to 3.9mm**	**51**	**-0.0411**	0.068	0.0095	-0.0597	-0.0225
3Y-6M	**> 3.9**	**31**	**-0.0637**	0.061	0.011	-0.0853	-0.0421

Change in ECC : Subjects with both 3 & 4 Year Follow-Up
Mean ECC at Preop = 2550
N=27

	% Loss/Gain
PreOp to 3 years	2.12%
PreOp to 4 years	0.47%
3 years to 4 years	-1.63%

1. **Do the endothelial cell data presented above in the overall analysis, stratified by anterior chamber depth and the extrapolations over time provide reasonable assurance of safety of the Artisan myopia lens?**

2. **Do the data presented in the PMA provide reasonable assurance of safety?**

3. **The proposed statement of indications reads: "The reduction or elimination of myopia in adults with myopia ranging from greater than –5 to less than –20 D with less than 2D of astigmatism at the spectacle plane; Patients with documented stability of refraction for the prior 6 months, as demonstrated by a spherical equivalent change of less than or equal to 0.50D."**

   Does the panel recommend any modifications to the proposed statement of indications with respect to:

   a). minimum anterior chamber depth (ACD's of <3.2 mm were excluded in the study),

   b). maximum pupil size (the 2 models of Artisan are intended for patients with pupil sizes up to 5.0 mm and up to 6.0 mm); and,

   c). minimum preoperative endothelial cell density? The outcomes of ECC changes reported in number 1 above could be used to determine acceptable minimum endothelial cell densities.

4. **Do the panel members have any additional labeling recommendations?**